

- 60 -

Claims

1. A DNA or RNA molecule which comprises a nucleotide sequence that encodes single-chain protein which is an agonist or antagonist of a hormone selected from the group consisting of luteinizing hormone (LH), follicle stimulating hormone (FSH), thyroid stimulating hormone (TSH) and chorionic gonadotropin (CG), which single-chain protein has an amino acid sequence of the formula

β -(linker)_n- α or

α -(linker)_n- β

10 wherein β is the β subunit of LH, FSH, TSH or CG or a variant thereof;

"linker" refers to a peptide linker containing 1-100 amino acids;

n is 0 or 1, and

α represents the amino acid sequence of the α subunit common to LH, FSH, TSH and CG or a variant thereof.

15

2. The DNA or RNA molecule of claim 1 wherein the nucleotide sequence encodes a protein wherein n is zero.

3. The DNA or RNA molecule of claim 1 wherein the nucleotide sequence encodes a protein wherein n is 1 and the linker is a complete CTP unit consisting of amino acid residues 112-118 to 145 of human chorionic gonadotropin β subunit.

20

~~4. The DNA or RNA molecule of claim 4 wherein the nucleotide sequence encodes a protein wherein n is 1 and the linker is a peptide containing 1-16 amino acids.~~

25

5. The DNA or RNA molecule of claim 6 wherein the nucleotide sequence encodes a protein wherein the linker is a glycine/serine repeat.

- 61 -

6. The DNA or RNA molecule of claim 1 wherein the nucleotide sequence encodes a protein wherein the α subunit or β subunit or both are modified by the insertion of a complete or partial CTP unit or variant thereof into a noncritical region thereof and/or wherein said linker includes a complete or partial CTP unit or variant thereof, wherein

5 CTP refers to the amino acid sequence found at the carboxy terminus of human chorionic gonadotropin β subunit which extends from amino acid residues 112-118 to residue 145, or a portion thereof or a variant thereof.

7. The DNA or RNA molecule of claim 1 wherein the nucleotide sequence

10 encodes a protein wherein said variants contain 1-5 conservative amino acid substitutions as referred to the native forms or are truncated forms of said sequences or both.

8. The DNA or RNA molecule of claim 1 wherein the nucleotide sequence encodes a protein wherein the α and β subunits are human α and β subunits or their

15 variants.

9. The DNA or RNA molecule of claim 1 wherein the nucleotide sequence encodes a protein wherein selected from the group consisting of formulas 1-10, 1a-10a, and 1b-10b of Table 1.

20

10. The DNA or RNA molecule of claim 1 wherein the nucleotide sequence encodes a protein wherein β is the β subunit of TSH or a variant thereof.

11. An expression system for the production of an agonist or antagonist of LH,

25 FSH, TSH or CG which comprises the nucleotide sequence of claim 1 operably linked to control sequences which effects its expression in a compatible host cell.

- 62 -

12. The expression system of claim 11 wherein the nucleotide sequence encodes a protein wherein n is zero.

13. The expression system of claim 11 wherein the nucleotide sequence
5 encodes a protein wherein n is 1 and the linker is a complete CTP unit consisting of amino acid residues 112-118 to 145 of human chorionic gonadotropin β subunit.

14. The expression system of claim 11 wherein the nucleotide sequence
10 encodes a protein wherein n is 1 and the linker is a peptide containing 1-16 amino acids.

15. The expression system of claim 11 wherein the nucleotide sequence encodes a protein wherein the linker is a glycine/serine repeat.

16. The expression system of claim 11 wherein the nucleotide sequence
15 encodes a protein wherein the α subunit or β subunit or both are modified by the insertion of a complete or partial CTP unit or variant thereof into a noncritical region thereof and/or wherein said linker includes a complete or partial CTP unit or variant thereof, wherein CTP refers to the amino acid sequence found at the carboxy terminus of human chorionic gonadotropin β subunit which extends from amino acid residues 112-118 to residue 145,
20 or a portion thereof or a variant thereof.

17. The expression system of claim 11 wherein the nucleotide sequence encodes a protein wherein said variants contain 1-5 conservative amino acid substitutions as referred to the native forms or are truncated forms of said sequences or both.

18. The expression system of claim 11 wherein the nucleotide sequence
25 encodes a protein wherein the α and β subunits are human α and β subunits or their variants.

- 63 -

19. The expression system of claim 11 wherein the nucleotide sequence encodes a protein wherein selected from the group consisting of formulas 1-10, 1a-10a, and 1b-10b of Table 1.

5

20. The expression system of claim 11 wherein the nucleotide sequence encodes a protein wherein β is the β subunit of TSH or a variant thereof.

10 11. 21. Recombinant host cells modified to contain the expression system of claim

12. 22. Recombinant host cells modified to contain the expression system of claim

15 13. 23. Recombinant host cells modified to contain the expression system of claim

14. 24. Recombinant host cells modified to contain the expression system of claim

20 15. 25. Recombinant host cells modified to contain the expression system of claim

25 16. 26. Recombinant host cells modified to contain the expression system of claim

17. 27. Recombinant host cells modified to contain the expression system of claim

112

08913238.082597

- 64 -

28. Recombinant host cells modified to contain the expression system of claim
18.

5 29. Recombinant host cells modified to contain the expression system of claim
19.

30. Recombinant host cells modified to contain the expression system of claim
20.

10

31. A method to produce an agonist or antagonist of LH, FSH, TSH or CG
which method comprises culturing the cells of claim 21 under conditions wherein said
agonist or antagonist is produced and
optionally recovering said agonist or antagonist from the cell culture.

15

32. A method to produce an agonist or antagonist of LH, FSH, TSH or CG
which method comprises culturing the cells of claim 22 under conditions wherein said
agonist or antagonist is produced and
optionally recovering said agonist or antagonist from the cell culture.

20

33. A method to produce an agonist or antagonist of LH, FSH, TSH or CG
which method comprises culturing the cells of claim 23 under conditions wherein said
agonist or antagonist is produced and
optionally recovering said agonist or antagonist from the cell culture.

25

34. A method to produce an agonist or antagonist of LH, FSH, TSH or CG
which method comprises culturing the cells of claim 24 under conditions wherein said
agonist or antagonist is produced and

- 65 -

optionally recovering said agonist or antagonist from the cell culture.

35. A method to produce an agonist or antagonist of LH, FSH, TSH or CG
which method comprises culturing the cells of claim 25 under conditions wherein said
5 agonist or antagonist is produced and
optionally recovering said agonist or antagonist from the cell culture.

36. A method to produce an agonist or antagonist of LH, FSH, TSH or CG
which method comprises culturing the cells of claim 26 under conditions wherein said
10 agonist or antagonist is produced and
optionally recovering said agonist or antagonist from the cell culture.

37. A method to produce an agonist or antagonist of LH, FSH, TSH or CG
which method comprises culturing the cells of claim 27 under conditions wherein said
15 agonist or antagonist is produced and
optionally recovering said agonist or antagonist from the cell culture.

38. A method to produce an agonist or antagonist of LH, FSH, TSH or CG
which method comprises culturing the cells of claim 28 under conditions wherein said
20 agonist or antagonist is produced and
optionally recovering said agonist or antagonist from the cell culture.

39. A method to produce an agonist or antagonist of LH, FSH, TSH or CG
which method comprises culturing the cells of claim 29 under conditions wherein said
25 agonist or antagonist is produced and
optionally recovering said agonist or antagonist from the cell culture.

- 66 -

40. A method to produce an agonist or antagonist of LH, FSH, TSH or CG which method comprises culturing the cells of claim 30 under conditions wherein said agonist or antagonist is produced and optionally recovering said agonist or antagonist from the cell culture.

5

08910228-082597

115